

## Section of the History of Medicine

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### Notes on Some Landmarks in Tropical Medicine

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PATRICK MANSON (1844–1922) is justly regarded as the father of modern tropical medicine. He was born of Scottish parents in the township of Old Meldrum, Aberdeenshire and educated at Aberdeen University. At 22 he migrated to Formosa, later moving on to Amoy in Southern China. Altogether he lived twenty-three years in China, practising latterly in Hong Kong for seven years.

In Amoy in 1877 he made his first momentous discovery of filarial periodicity. The filarial embryo had been demonstrated by Timothy Lewis (1841–1886), some five years previously, but it was left to Manson to point out the true implication of its appearance in the blood-stream at night-time only, and the bearing of this phenomenon upon the life-history of the parasite. He argued then, that this was a habit-adaptation to that of the night-feeding brown mosquito of Amoy (*Culex pipiens*). In 1879 he proved this. He found that the mosquito served in the capacity of a “nurse”, or what is now known as an intermediary host. The filaria underwent development in the thoracic muscles of this insect, becoming completely changed in appearance during this process.

Amongst Manson's relics at his death was a letter from Timothy Lewis, dated January 14, 1878, expressing his appreciation of Manson's communications, but warning him against unhesitatingly regarding the minute filariae he had found in the tissues of the mosquito as developmental stages, as they might prove to be special nematode parasites peculiar to these insects (a fact which is now known to be true). Lewis, however, judging by his own personal dissection of mosquitoes, could find no morphological differences between them and the embryo of *Filaria sanguinis hominis*.

Lewis was shortly after recalled to Netley, where he organized the pathological department there and did signal service. He was also closely associated with D. D. Cunningham (1843–1914), the discoverer of *Entamoeba coli*, as well as of the parasite of oriental sore, which he recognized, but did not name.

Manson was in correspondence with T. Spencer Cobbold (1828–1886), who as the most distinguished helminthologist of his time, was the recipient of specimens collected all over the world. It was Cobbold who named *Filaria bancrofti*, *Bilharzia hæmatobia*, and many other parasites. His appointments were curiously diverse: he was working at geology in the British Museum, and at parasitology at the Middlesex Hospital, as well as at the Veterinary College. It was his privilege to present Manson's communications to the Linnaean Society and to the Queckett Microscopical Club. Hence the following story:—

On June 20, 1879, Manson wrote to Cobbold an account of his experiments and forwarded him filaria-impregnated mosquitoes preserved in glycerine and fed on the

blood of his Chinese gardener, who was heavily infected. There were five glass bottles filled with specimens and adequately labelled. The letter ends as follows :—

“ It seems to me that Lewis by his great discovery has opened a new field in tropical pathology. Men like myself, in general practice, are but poor and very slow investigators, crippled as we are, with the necessity of making our daily bread.”

These were evidently the specimens which were demonstrated by Cobbold to the Medical Society of Middlesex Hospital in February 1884, before a large audience. The leather case containing these mosquitoes intact, just as they left Amoy in 1879, was rediscovered in the Royal College of Surgeons by Prof. R. T. Leiper, in 1935.<sup>1</sup>

Manson in later years (1895), being in need of some infected mosquitoes, ransacked London for them in vain. In a letter to Ronald Ross, on December 23, 1895, he wrote :—

“ I have at last succeeded in getting a filariated mosquito. Many years ago—seventeen or eighteen—I sent to Cobbold a lot of filariated mosquitoes. I knew that Cobbold’s collection had gone to the College of Surgeons, and so got permission to look over them for my mosquitoes, but failing, I went to Stephen Mackenzie, and there found a small bottle with a solitary mosquito floating in glycerine. In a section of the blood in its abdomen there were my Amoy filariæ, and in its thoracic muscles they were too, most beautiful to behold.”

This was evidently one insect of this batch which has been so dramatically rediscovered.

Joseph Bancroft (1836-1894), the discoverer of the adult form, *Filaria bancrofti* (so-named by Cobbold) was an Englishman who settled in Brisbane in 1864. He never communicated directly with Manson, though his son, Thomas Bancroft, in 1899, consigned to Manson infected mosquitoes preserved in glycerine, and these were the insects which were sectioned in celloidin by Dr. G. Carmichael Low in the following year, whereby the complete life-history of the larva was unfolded and its presence in the proboscis of the insect demonstrated. This showed that the mosquito conveyed the parasite in the act of biting—a mode of communication which had been suggested by Cobbold himself in a review in the *Veterinarian* as far back as March 1883, though somehow or other, this suggestion had not been acted upon. We do know, however, that the elder Bancroft, writing to Cobbold in the spring of 1877, expressed his *belief* that mosquitoes would be found to convey filariasis, but his own examinations had proved entirely inconclusive in that direction.

It is fortunate for posterity that Manson kept a scientific diary (now preserved in Manson House) commencing in June 1877 and continuing to 1896. It consists of 615 closely written pages and contains an account of his major discoveries, and from it many historical data have been culled. In 1887 Manson visited Li Hung Chang, who was said to be suffering from cancer of the tongue. Luckily it was only a sub-lingual abscess, which was successfully opened. On returning he received this gracious letter from the great statesman.

“ *Li Hung Chang to Patrick Manson.*

4th December, 1887.

“ On account of a recent slight malady at the root of my tongue I have had the honour to receive your visit from afar. My thanks I am unable to express, and your treatment has already resulted in a complete cure. Calm, then, your anxiety on my account. I send you enclosed a photograph which may perhaps

<sup>1</sup> The actual specimen was exhibited at the meeting.

serve as a reminder of the sincerity of our good feelings towards one another ; and I hope you will accept it. This is the object of my letter and I take this opportunity of wishing you an elegant time. My card is enclosed.

Kuang Hsii, 13th year, 10th moon and 20th day."

The story of the discovery of the lung fluke—*Paragonimus westermanii* (then designated by Cobbold *Distoma Ringeri*)—is also a romance and is related in the *Diary*. On April 24, 1878 a mandarin consulted Manson on account of some eczematous eruption, but, whilst speaking, he hawked up a small quantity of reddish sputum and it was noted that his voice was rough and loud. Observing that the sputum was tinged with blood, Manson immediately seized a portion with his forceps and put it under his primitive microscope to look for filariæ (which he then believed sought to leave the body by this route) but he was surprised to find eggs of a hitherto undiscovered parasite. Immediately he communicated his discovery to Dr. Ringer, a correspondent in Formosa, and besought him to investigate a Portuguese patient who, suffering from a thoracic aneurism, had left Amoy Hospital and returned to Formosa. At the autopsy on this man Dr. Ringer found a parasite, the size of a pea, in the lung and forwarded it in spirit to Manson, who was delighted to observe in the sediment of the bottle, ova similar to those in the sputum of the Chinese patient already noted. The parent worm was then sent to Cobbold who recognized it as a new species and named it *Distoma Ringeri*.

Later Manson made observations on these eggs, kept for various periods in water in order to elucidate their life-history. He was able to observe, after many weeks, the liberation of the miracidium, and made several shrewd guesses at its life-history which, however, was not fully worked out till thirty-five years later by Nakagawa.

The first intermediary of *Paragonimus* is now known to be a freshwater mollusc—*Melania libertina* (Gould), and yet we find in the *Diary* a letter from a conchologist, R. Hungerford, dated October 21, 1881, suggesting that this snail acted as carrier in the transmission of this trematode. No further notice of this pregnant suggestion appears to have been made at this time, and a valuable hypothesis remained abortive.

The most amazing part of these fundamental discoveries is that they were made without any recourse to post-mortem material. Thus we find Manson writing :—

"The difficulties of obtaining post-mortem examinations were insuperable. One of my filaria patients was dying of an intercurrent disease. Being eager to find the parental form, I offered him 200 dollars to be handed to his widow for permission to perform a post-mortem dissection of his body. He agreed and a proper document was drawn up. On his death the widow claimed the money and I was allowed to dissect the body. My brother and I proceeded to the man's house in the very heart of the native town, prepared to spend several hours in search of the parental filaria (which had then not been discovered). I had barely commenced the section when we heard an ominous noise outside. A mob had gathered and was anxious to know what the 'foreign devils' were doing. We had to run for our lives, and I lost my two hundred dollars. Being denied the opportunity of necropsies in man, I had to make use of dogs, cats, and birds of various sorts. In the course of these examinations a great variety of hæmatozoal parasites were found. I had found that the blood of the magpie contained at least two species of filaria, so I procured as many of these birds as possible, but the Chinese told me I must stop my work in this direction, because the magpie is a sacred bird in China, tradition holding that, many years ago, the spirit of a defunct Emperor had entered one of these birds. Therefore it was possible that either I, or my friends, might shoot this particular fowl. I don't know that this absolutely deterred me, but the birds themselves

which, under ordinary circumstances, are remarkably tame in China, soon got to know that I was after them."

Manson's part in the mosquito malaria hypothesis, as it was then called, is so well known that it hardly bears repetition. Manson's long connexion with Ronald Ross commenced in April 1894 in London and their original correspondence is preserved *in toto*. The first letter from Manson to Ross is dated April 9, 1894, and in it he explains to his pupil that the reason why he has not recognized the malaria parasite is because he has not used the proper technique.

The debt Ross owed to Manson was expressed in 1898 when he wrote :—

"These observations prove the mosquito theory, as expounded by Dr. Patrick Manson, and in conclusion, I should add that I have consistently received the benefit of his advice during the enquiry. His brilliant instruction so accurately indicated the true line of research that it has been my part merely to follow its direction."

Finally, Manson's maxim of research should be engraved on the walls of every scientific laboratory. It runs as follows :—

"Never refuse to see what you do not want to see, or what might go against your own cherished hypothesis, or against the view of authorities. These are just the clues to follow up, as is also, and emphatically so, the thing you have never seen or heard of before. The thing you cannot get a pigeon-hole for is the finger-point showing the way to discovery."